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Abstracts

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Is membranoproliferative glomerulonephritis (MPGN) really decreasing? A multicentric study of 1548 patients with primary GN. *R. Confalonieri, M. Baroni, B. Pagliari, M. L. Lavagni, M. T. Porri, G. Banfi, E. Imbasciati, G. Colasanti, and G. Barbiano di Belgiojoso. Renal Units, Ospedale Maggiore Policlinico, Niguarda-Ca'Granda and S. Carlo Borromeo, Milan, Italy.* Some authors reported that the incidence of MPGN within primary GN showed a reduction in the last decade. To confirm such observation and to characterize the variations of MPGN incidence with time, 1548 renal biopsy specimens from patients with primary GN from January 1972 to December 1983 have been reviewed. The series was obtained combining the experience of three nephrological units in the same city. The study included patients with focal glomerulosclerosis (FGS 286 patients), membranous GN (MGN 315 patients), diffuse proliferative GN (AGN 185 patients), diffuse crescentic GN (CGN 101 patients), IgA nephritis (IgAGN 457 patients), and MPGN (204 patients). Most patients had been diagnosed by means of both light microscopy and immunofluorescence. To reach a confirmed histological diagnosis and a homogeneous morphological evaluation, biopsy specimens prior to 1972 were excluded, as well as patients with minimal changes, advanced sclerosing GN, and unclassable forms. GN secondary to systemic disease have been excluded as well. Statistical analysis has been performed by the X^2 method. A progressive decrease of number of MPGN was observed, despite the increased total number of biopsy specimens. For simpler statistical examination, comparison was made between three periods of 4 years each. The incidence of MPGN was significantly lower for each of the three periods if compared with the preceding one ($P < 0.01$ for period 1 vs. 2 and $P < 0.001$ for 2 vs. 3). The percent of MPGN was 21%, 14%, and 6% for the three periods, respectively. Only FGS had a significant increase for the third period if compared with the second one. No significant difference between the three periods has been observed regarding sex, age, nephrotic syndrome, or hypocomplementemia at observation. The number of type 2 MPGN for each period showed no change, thus having an increased incidence (6%, 10%, and 18%, respectively). No modification within the total number of biopsy specimens was found. The observation agrees with another study performed in the Paris, France, area. The nature of the modified incidence is obscure. Exogenous or environmental factors influencing large population areas such as a possible decrease of etiologic agents can be postulated.

Macrophage Fc-receptor function in idiopathic glomerulonephritis. *D. Roccatello, R. Coppo, G. Martina, C. Rollino, B. Basolo, F. Quarello, G. Picciotto, P. G. De Filippi, D. Cordonnier, and G. Piccoli. Chair of Medical Nephrology of University of Turin, Nephrology and Dialysis Units and Nuclear Medicine Department, S. Giovanni Hospital, Turin, Italy, and Centre Hospitalier Universitaire, Grenoble, France.* Experimental models suggest that the mononuclear phagocyte system (MPS) plays a key role in nephropathies having an immune pathogenesis. Methods for studying MPS immune function in vivo have only recently been developed and data in idiopathic glomerulonephritis (GN) are scanty. We examined 48 patients: 17 membranous GN (MGN), 8 membranoproliferative GN (MPGN), 7 focal glomerulosclerosis (FGS), and 16 primary IgA nephropathy (IgA-N). No patient was under treatment with steroids or immunosuppressive drugs. MPS Fc-receptor function was detected as described by Frank by measuring the half-life (t 1/2) of autologous IgG-sensitized red blood cells (RBC) labelled with ^{51}Cr (normal values: 31 ± 6.37 min). A MPS dysfunction was found in 62.5% of the patients with nephrotic range proteinuria and/or severe microhematuria, but in only one out of 16 patients with minimal or absent urinary abnormalities (proteinuria <0.7 g/day, hematuria <5 RBC/high power microscopic field). Mean t 1/2 values were significantly higher than the 95th percentile of those in 14 normal subjects with MPGN (44.1 ± 14 min, $P < 0.05$) and IgA-N (55.7 ± 41.6 min, $P < 0.025$). A significant correlation was found, in MPGN, between t 1/2 and proteinuria levels ($r = 0.7$, $P < 0.05$). In MGN t 1/2 values (47.2 ± 34 min) were not different from those of normal controls. However, a delayed immune clearance was observed in 7 of 17 patients. Only one out of seven FGS patients had an impaired MPS function. In IgA-N a good correlation ($P < 0.05$) was found between levels of IgA containing immune complexes (as detected by a conglutinin solid phase test) and those of t 1/2. Conversely, no correlation was observed between values of t 1/2 and levels of IgG immune complexes (C1q solid phase test) in any patient group. Our results suggest that an impairment of Fc-receptor MPS function is a frequent feature in patients with idiopathic GN and urinary findings of active disease. The mechanism responsible is uncertain. However, a MPS dysfunction might favor the persistence of immunologically active substances in the bloodstream and possibly their deposition in the kidney.

The detection of monocytes in essential cryoglobulinemia-associated glomerulonephritis (GN): histochemical analysis in 29 patients. *F. Ferrario, A. Castiglione, G. Colasanti, G. Barbiano di Belgioioso, C. Brunati, S. Nava, and G. D'Amico. Divisions of Nephrology, San Carlo and Ca' Granda Hospital, Milan, Italy.* The participation of monocytes in the immunopathogenesis of experimental GN seems well established. More recently, the presence of intraglomerular monocytes has also been reported in human GN, especially in cases associated with essential cryoglobulinemia (EC). To evaluate the presence and the possible role of these cells, we examined cryostatic sections of renal biopsy specimens from 29 patients with EC-associated GN, by means of nonspecific esterase (NSE) reaction for monocytes. The number of NSE-positive cells per glomerulus has been evaluated in all patients, obtaining a mean index of intraglomerular monocytes (M/G) for each biopsy. The mean value of M/G in this disease was particularly high (30.6 ± 22.4), and it was significantly different according to histological subgroups: *(1)* diffuse proliferative GN with "thrombi" = 9 patients, M/G 54.2 ± 12.5; *(2)* diffuse proliferative GN without "thrombi" = 10 patients, M/G 32.1 ± 14.2; *(3)* lobular GN = 4 patients, M/G 8.4 ± 5.8; *(4)* focal proliferative GN = 6 patients, M/G 6.6 ± 6.5 (1 to 2, 2 to 3, 2 to 4 = $P < 0.01$; 1 to 3, 1 to 4 = $P < 0.001$). In diffuse GN with "thrombi" interposition of monocytic cytoplasm within glomerular basement membranes as well as a close relationship between monocytes and "thrombi" were frequently observed. Moreover, serial biopsy specimens in two such patients showed a disappearance of both monocytes and endoluminal "thrombi." The amount of proteinuria was the only clinical parameter correlated (although not to a significant level) with the degree of monocyte infiltration. In the 12 patients with M/G > 40, mean proteinuria was 4.9 ± 5.0 g/24 hr; in the 9 patients with M/G between 10 and 40, mean proteinuria was 3.4 ± 2.3 g/24 hr; in the 8 patients with M/G < 10, mean proteinuria was 1.2 ± 1.5 g/24 hr. Our results confirm a high degree of monocyte infiltration in EC-associated

GN. In particular the strict relationship between monocytes and cryoprecipitates ("thrombi") suggests immune adherence mechanisms as a modality of intraglomerular recruitment of these cells and their possible phagocytic capacity on deposited immune-complexes. Finally, the correlation between M/G and proteinuria confirms experimental data on the active role of monocyte/macrophage cells in inducing a glomerular damage and determining permeability alterations of the glomerular basement membrane.

The correlation between proteinuria and intraglomerular monocytes in proliferative glomerulonephritis (GN). *F. Ferrario, A. Castiglione, G. Colasanti, M. G. Lavagni, S. Bertoli, S. Nava, and G. D'Amico. Divisions of Nephrology, San Carlo and Ca' Granda Hospitals, Milan, Italy.* Recent studies in experimental GN showed a close relationship between intraglomerular monocyte infiltration and proteinuria: the role of these cells in the pathogenesis of tissue damage is actually under active investigation. To establish a possible correlation between proteinuria and degree of monocyte infiltration also in human GN, we analyzed 124 cases of biopsy-proven proliferative GN, classified as follows: 61 systemic lupus-associated GN, 27 acute post-infectious GN, 19 crescentic GN (>80% of glomeruli with circumferential crescents), 17 membranoproliferative GN. To identify monocytes, a histochemical method of esterase was used on cryostatic sections; the number of esterase-positive cells per glomerulus has been evaluated in all cases, obtaining a mean index of intraglomerular monocytes (M/G) for each biopsy. The patients have been further divided according to the presence of severe (M/G > 5) or moderate (M/G < 5) monocyte infiltration and a highly significant correlation between the number of esterase positive cells and the amount of proteinuria has been found in each group of GN.

	M/G > 5		M/G < 5		
	No. of cases	Proteinuria *g/24 hr*	No. of cases	Proteinuria *g/24 hr*	Student's *t* test
Lupus GN	27	2.9 ± 2.5	34	1.4 ± 1.3	$P < 0.01$
Acute post-infectious GN	18	2.4 ± 2.0	9	0.8 ± 0.5	$P < 0.05$
Crescentic GN	11	5.7 ± 2.0	8	2.1 ± 1.3	$P < 0.01$
Membrano-proliferative GN	5	7.3 ± 5.9	12	3.1 ± 1.8	$P < 0.02$

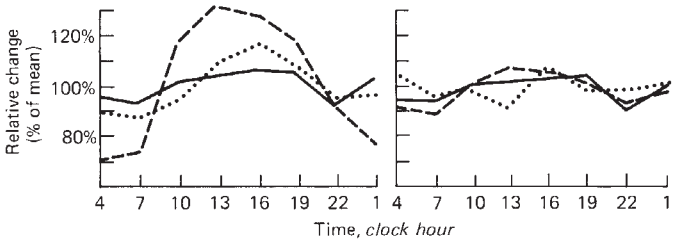
Our results suggest that among multiple mechanisms leading to proteinuria, monocyte may play a direct role in inducing glomerular damage, possibly through the release of lytic enzymes to glomerular basement membrane.

The action of thyroid hormones on sodium proximal tubule transport. Effect on Na-K-ATPase activity in isolated single nephrons. *G. Capasso, R. Kinne, N. G. De Santo, and C. Giordano. Albert Einstein College of Medicine, New York, New York, USA, and I° Faculty of Medicine, Naples, Italy.* Our previous studies demonstrated that fluid reabsorption (J_v) by the late proximal convoluted tubule of chronically thyroidectomized rats (TX) is reduced compared to control and is doubled by the administration of low doses (10 μg/kg/bw) of triiodothyronine (T_3) for 3 days (TX + T_3). To determine if the latter was due to an increased Na-K-ATPase activity, enzyme activities were measured in single tubule segments using a kinetic micro assay. Early (S_1) and late (S_2) proximal tubule segments were isolated from the cortex of collagenase-perfused kidneys of control, TX and TX + T_3 rats. The results are summarized in the table and expressed as picomoles of ADP generated per minute per millimeter of tubule length (mean ± SEM, N = number of rats, $^*P < 0.005$ vs. TX).

	Control	TX	TX + T_3
S_1	156.1 ± 16.8*	68.4 ± 8.9	55.6 ± 6.9
N	(7)	(6)	(5)
S_2	50.3 ± 4.8*	16.6 ± 4.1	17.0 ± 3.7
N	(9)	(8)	(5)

The data show that Na-K-ATPase decreases following chronic thyroidectomy, but that administration of low doses of T_3 increases J_v without a change in Na-K-ATPase activity. This discrepancy between Na-K-ATPase activity measure in vitro and J_v determined in vivo might indicate that low doses of T_3 do not affect Na-K-ATPase activity directly, but stimulate tubular transport by a different mechanism.

Diurnal variation of urinary total protein (P) and albumin (A) excretion. *L. Arisi, F. Capani, R. Barani, A. La Russa, S. Alfieri, and C. Buzio. Clinica Medica e Nefrologia, Università di Parma, Parma, Clinica Medica Generale, Università di Chieti, Chieti, Italy.* Day-time orthostatic P and A excretion is known to exceed night-time clinostatic excretion. The changes of posture and activity are generally agreed to be causative. But when recumbency is maintained over 24 hr, the day-night differences persist, suggesting that other mechanisms play a role. To improve our knowledge of the behavior of P and A excretion, we measured it, together with that of creatinine, in eight consecutive urine specimens carefully collected for 3-hr periods from normal subjects (group 1; N = 16) and nephropathic patients (group 2; N = 12) maintained at bedrest for 24 hr. P was measured by the amido-black method according to Heremans, A by electroimmunodiffusion method according to Laurell, urine creatinine (Cr) by standard autoanalyzer. In all subjects, the values of P, A, and Cr obtained in each single 3-hr period were expressed as percents of their mean values of the eight periods. The time relation to the average relative changes of P (−) A (--) Cr (...) is shown in Figures 1 (left, group 1) and 2 (right, group 2). Furthermore, statistical analysis by means of the paired t test was performed comparing the mean value for each 3-hr period with the corresponding preceding value. Both groups show identical timing in P, A, and Cr maximal excretion rates, but only group 1 shows significant variations of P and A before and after the sole significant variation of Cr. The last one was the only significant finding recorded in group 2. In conclusion, in normal subjects, non-syncronous circadian rhythms regulate urinary excretion of P, A, and Cr, independently of posture changes. In nephropathic patients Cr rhythm is maintained while the P and A ones are lost.



The dopaminergic response of patients with liver cirrhosis. *A. Morganti, G. Graziani, F. Salerno, P. L. Incerti, G. Bolla, E. Lorenzano, S. Casati, and P. Ghirardi. Institutes of Clinica Medica III and IV, University of Milan, Department of Nephrology, Ospedale Maggiore and Medical Research Unit, SIMES, Milan, Italy.* The hyponatriuria that is commonly found in patients with advanced liver cirrhosis (ALC) is reversible on long-term infusion of dopamine. To investigate the response of vascular and tubular dopamine receptors to Ibopamine (I), an orally active dopamine derivative, we measured urinary flow (U ml/min), glomerular filtration rate (GFR ml/min), fractional excretion of sodium and potassium (FeNa% and FEK%), plasma renin activity (PRA ng/ml/hr), and urinary aldosterone excretion (UA ng/min) before and after the administration of 50 mg I in 11 patients with ALC. Blood and urine samples were collected prior to (time 0) and 80, 160 and 240 min after I. The results are reported in the table (one asterisk indicates $P < 0.05$).

Time	V	GFR	FeNa
0	0.7 ± 0.1	120 ± 10	0.09 ± 0.03
80′	2.1 ± 0.4*	261 ± 31*	0.15 ± 0.04
160′	1.1 ± 0.2	136 ± 17	0.35 ± 0.08*
240′	1.2 ± 0.3	128 ± 26	0.37 ± 0.11*

Time	FeK	PRA	UA
0	5.9 ± 0.6	1.7 ± 0.6	24 ± 7.0
80′	9.1 ± 1.3*	0.9 ± 0.2*	47 ± 10*
160′	11 ± 1.7*	0.9 ± 0.3*	23 ± 8.0
240′	8.8 ± 1.5*	0.9 ± 0.3*	25 ± 7.0

These data indicate that the acute stimulation of the renal dopaminergic receptors by I results in a significant natriuretic effect. This may be due to independent vascular and tubular mechanisms since the changes in GFR tend to disappear when those in FeNa become more evident.

Endogenous opioids and baroreflex control of heart rate in chronic uremic patients. *C. Zoccali, F. Mallamaci, M. Ciccarelli, and Q. Maggiore. Centro Fisiologia Clinica CNR, Reggio Calabrie, Italy.* Baroreflex control of heart rate is abnormal in patients with chronic renal failure, but the cause of this dysfunction is unknown. The endogenous opioid Metenkephalin, which has a depressant action on baroreflex sensitivity and is markedly elevated in plasma of chronic uremics, could be responsible for the baroreflex dysfunction. To evaluate this hypothesis, we tested the effect of the opiate antagonist Nalaoxone (0.07 mg · kg^{-1}) on the response to Valsalva maneuver in nine uremic patients (UP) on chronic dialysis and in seven healthy subjects (HS) matched for age and sex. The experimental design was single-blind, placebo-controlled, randomized, crossover, and balanced. In UP Naloxone caused a progressive increase in Valsalva maneuver ratio from a subnormal control value of 1.46 ± 0.09 (SEM) to a final value (3 hr) of 1.73 ± 0.11 ($P < 0.0125$ by repeated measures ANOVA); in HS the drug had no effect (control:1.75 ± 0.15; 3 hr:1.73 ± 0.12). The placebo did not cause any change in either group. The increase in Valsalva maneuver ratio after Naloxone observed in UP was due to lengthening of the RR interval during the release phase (longest RR:control 850 ± 120 msec, 3 hr 980 ± 70 msec; $P < 0.01$) indicating an enhanced parasympathetic activation. Strain phase RR interval changes were unaffected by the drug. In conclusion, by enhancing the parasympathetic activation of the release phase, Naloxone restores the subnormal Valsalva maneuver ratio of chronic uremic patients. This effect is likely due to antagonism of the depressant effect of Metenkephalin on baroreflex sensitivity. Elevated plasma levels of Metenkephalin may be responsible for the baroreflex dysfunction of uremic patients.

3,3′,5′ Triiodothyronine (reverse T3) and glucose intolerance in uremia: evidence of a useful indicator of carbohydrate metabolic control. *S. De Marchi, E. Cecchin, and F. Tesio. Department of Internal Medicine, Hospital of Codroipo (Udine), Codroipo Unit of Nephrology and Dialysis, Hospital of Pordenone, Pordenone, Italy.* In endstage renal disease glycosylated hemoglobins are not useful parameters of long-term carbohydrate metabolic control. Recently low triiodothyronine (T3) and raised 3,3′,5′ triiodothyronine (reverse T3 or rT3) levels have been reported in uncontrolled diabetes mellitus. Thyroid status has been extensively investigated in chronic renal failure. Previous studies reported that serum T3 and thyroxine (T4) concentrations are below the normal range in about one third of uremic patients. Little is known about rT3 whose serum levels have been found to be either normal or low or increased in uremia. The aims of this study are to further elucidate these apparently controversial reports on rT3 in chronic renal failure by attempting to assess the relation between plasma glucose and thyroid hormone concentrations and to investigate the possibility that rT3 may be an indicator of long-term carbohydrate metabolic control in uremic patients on hemodialysis. We measured pre-dialysis serum levels of T3, T4, rT3, TSH, insulin, glycemia, and glycosylated hemoglobins (HbA1 and HbA1c) in 30 patients with endstage renal disease receiving long-term hemodialysis. An oral glucose tolerance test (OGTT) was performed in all patients: 16 had a normal glucose tolerance (NGT), and 14 had an impaired glucose tolerance (IGT) according to the NDDG's criteria. Serum T4 and T3 levels were significantly reduced in uremic patients as compared with those of a control group of 30 subjects well matched for age and sex. TSH levels showed no difference between patients and controls. Reverse T3 values varied considerably among patients being either normal or low or slightly increased. There was no difference in the mean values of T3 between patients with IGT and NGT. Contrarily rT3 was significantly increased in patients with IGT as compared with those with NGT (0.215 ± 0.039 vs. 0.124 ± 0.016 ng/ml; $P < 0.0001$). Reverse T3 showed positive relationships to pre-dialysis glycemia ($P = 0.005$) and to the glycemic peak during the OGTT ($P = 0.005$); furthermore it correlated to pre-dialysis insulinemia ($P = 0.0017$) and to the insulinemic peak during the test ($P < 0.0001$). In contrast these parameters of carbohydrate metabolic control did not correlate with T3 and glycosylated hemoglobins. No correlation was found between rT3 and dialytic age. In conclusion, these data might explain, at least in part, the contrasting reports on rT3 levels in uremia suggesting that it may be a useful indicator of carbohydrate metabolic control in patients with endstage renal disease receiving long-term hemodialysis.

A new method for insertion of indwelling peritoneal dialysis catheter (PC). *N. Di Paolo, A. Manganelli, F. Strappaveccia, M. De Mia, and E. Gaggiotti. Nephrology Department, Regional Hospital of Siena, Siena, Italy.* To eliminate the discomfort caused by surgical methods and the risk involved using the Trocar, we have used a new technique for insertion of the PC for 1 year. We devised a steel instrument, vaguely resembling a rinoscope, composed of 2 semicones either 6 or 7.5 cm long with a rounded tip. The handles are connected by a screw to permit dilatation of semicones. After a local anesthesia, an introducer needle is inserted into the peritoneal cavity. A guidewire is passed through the needle which is then withdrawn and the instrument is placed around the guide and gently pushed up to the peritoneal cavity. The guide is then removed and squeezing the handles of the instrument, we introduce the PC up to 2 cm beyond the first dacron cuff. Once the PC is in place, the instrument is removed and a subcutaneous tunnel may be made. There is a possibility that the needle may perforate an intestinal loop, but when experimenting on dogs we observed that, in this case, the instrument will press down the loop without piercing, and when the guide is withdrawn, it remains in the abdominal cavity and the PC will assume the correct position. We have used this method for 25 patients. Fourteen were new patients while 11 underwent the PC repositioning. For all patients this new method proved to be excellent with no leakage and PCs were utilized after only 24 hr. We emphasize the brief time for PC insertion, the minimum discomfort, and simplicity of the technique.

Pregnancy in women with chronic renal failure (CRF). *E. Imbasciati, P. Bozzetti, M. L. Airoldi, G. C. Ambroso, B. Pagliari, G. Pardi, E. Massa, and P. Capetta. Divisione Nefrologia Ospedale Maggiore, Clinica Ostetrica e Ginecologica I e II, Università di Milano, Milano, Italy.* The course of pregnancy (P) and its effect on renal disease in women with CRF has been studied only in a few patients. The high rate of fetal loss and worsening of renal function are reported. We describe 18 P in 18 patients with renal disease and serum creatinine ≤1.6 mg/dl before P. Six patients had chronic glomerulonephritis; five, interstitial nephritis; two, vascular disease; and five, undefined etiology. There were two spontaneous abortions, two therapeutic abortions, one stillbirth, and 13 livebirths, six of them before the 36th week. Cesarean section was done in 7 patients. Fetal weight was greater than 2500 g in five newborns. Eight patients were hypertensive before P and two became hypertensive during P. The effect of P on progression of renal failure was evaluated in 13 patients in whom it was possible to calculate the linear regression of reciprocal serum creatinine before and after P. In eight patients the rate of progression did not change after P. One of them had a marked increase of serum creatinine during P which reversed after delivery. In three patients a decline of renal function occurred during P and continued after delivery (two patients) or after abortion (one patient). In two patients renal function remained stable during P and progressively worsened after delivery. Arterial hypertension was present before P in four of five patients who worsened and

in three of eight who did not. In conclusion, P in women with CRF may end in a successful delivery, but it may be accompanied by a worsening of renal function especially in hypertensive women.

The dopaminergic stimulation of transplanted kidney. *G. Graziani, F. Egidi, A. Morganti, C. Sala, F. Salerno, P. L. Incerti, E. Lorenzano, P. Passerini, P. Ghirardi, and C. Ponticelli. Divisione di Nefrologia e Dialisi Ospedale Maggiore, Clinica Medica III e IV Università, Sez. Ricerche Simes, Milano, Italy.* The stimulation of renal vascular and tubular dopaminergic receptors increases urinary flow, glomerular filtration rate and the fractional excretion of sodium and potassium. To investigate either the role of renal innervation or of the renal mass reduction in response to an acute dopaminergic stimulation, 50 mg of Ibopamine, an orally active dopamine derivative, were administered to nine cadaveric transplant patients (TX), with normal and stable blood creatinine levels, three subjects who had donated one kidney for transplant (D) and the three related transplant recipients with a denervated kidney (R). The results were compared to those observed in six healthy volunteers (C). Urinary flow (UV ml/min), glomerular filtration rate (GFR ml/min), fractional excretion of Na and K (FeNa% and FeK%), and plasma renin activity (PRA ng/ml/hr) were measured before (time 0) and every 80 min after Ibopamine administration. In the table, ** indicate $P < 0.001$ and * $P < 0.05$ in respect to time 0.

	UV		GFR	
Time	TX	C	TX	C
0	1.10 ±0.4	0.87 ±0.4	94.7 ±35	104.6 ±24
80′	0.95 ±0.3	3.31* ±2.0	101.6 ±39	206.1** ±51
160′	0.82 ±0.2	1.85 ±0.5	70.0 ±14	87.5 ±17
240′	1.29 ±0.5	2.33 ±1.6	82.5 ±22	93.6 ±26

	FeNa%		FeK%		PRA	
Time	TX	C	TX	C	TX	C
0	1.0 ±0.5	0.87 ±0.4	11.7 ±4.8	6.3 ±1.4	2.5 ±1.4	0.5 ±0.5
80′	0.8 ±0.3	1.27** ±0.4	13.2 ±8.5	13.5** ±5.1	2.6 ±1.6	0.3 ±0.2
160′	1.1 ±0.5	1.36** ±0.4	16.4 ±7.5	13.3* ±6.1	2.6 ±2.1	0.2 ±0.1
240′	1.4 ±0.5	1.30** ±0.4	20.4* ±16.8	10.7* ±4.9	3.0 ±1.6	0.2 ±0.1

The three D showed the same response of R and TX to dopaminergic stimulation. In conclusion, uninephrectomized innervated or denervated patients showed submaximal glomerular hyperfiltration, since GFR failed to increase in response to vascular receptors stimulation. Ibopamine promoted Na and K excretion, by tubular receptors stimulation, the latter becoming active also in denervated kidney. This natriuretic and kaliuretic effect seems not to depend on GFR or PRA modifications. The neural control of the kidney does not appear to play a role in mediating the renal response to dopaminergic stimulation.

Erythroid colony formation in renal transplantation patients with erythrocytosis. *S. Lamperi and S. Carozzi. Division of Nephrology, St. Martin Hospital, Genoa, Italy.* In 55 renal transplantation patients, erythrocytosis (E) was observed in six subjects with hematocrit (Hct) and hemoglobin (Hb) mean values, respectively, 59 ± 2% and 19 ± 1 g/dl. All patients showed normal serum creatinine, blood pressure, and respiratory function. In all patients, with or without E, the growth of erythroid progenitor cells (BFU-e) drawn from peripheral blood was evaluated in in vitro cultures. Moreover, in the same subjects, the serum erythropoietin (S-Ep) levels by fetal mouse liver cell assay were evaluated. The results showed a significant increase on the basal values of S-Ep in E and in non-E patients, respectively, 400% and 492%, with a subsequent decrease when Hct and Hb reached steady high levels, showing that a feedback control system was restored in most of the transplanted patients. Notwithstanding the diminution of S-Ep, on the contrary, six patients demonstrated a further progressive rise of Hct and Hb levels up to reach an erythrocytosic state. In in vitro cultures the peripheral BFU-e of these patients, showed a noticeable sensitivity to the progressively reduced doses of Ep and also to be capable of developing a few colonies per plate when the medium was Ep free, while in non-E patients, the BFU-e growth needed the addition of the high dose of Ep. These results were not verified using peripheral blood depleted of monocyte and/or T-lymphocyte cells. Therefore, in transplanted patients with E it is possible that particular cellular interactions and/or the product of their secretion stimulate an early hyperproliferation of BFU-e with a greater Ep sensitivity but at least partly with the capacity of growing also in the absence of Ep.

Cytoplasmic free (Ca^{2+}) in blood cells in hypertension (HT). *G. Bruschi, A. Cavatorta, M. E. Bruschi, C. Pavarani, G. Orlandini, M. Spaggiari, M. Caroppo, L. Tacinelli, and A. Borghetti. Medical Clinic and Nephrology, University of Parma, Parma, Italy.* There have been reports suggesting an altered control of cellular calcium in HT. However, the cytosolic-free calcium concentration (the pool playing the vital role in regulating many cell activities) has never been measured reliably and nondisruptively in small blood cells. We used the membrane-permeant fluorescent Ca indicator Quin 2. Data on platelets and lymphocytes of essential hypertensive patients (EHP), normotensive control subjects (NCS), spontaneously hypertensive rats (SHR), and Wistar-Kyoto rats (WKY) at different ages are illustrated in the table below. All results are expressed in nmoles/liter as mean ± SEM.

	Lymphocytes	*P*	Platelets	*P*
EHP	120.5 ± 4.8	NS	144.9 ± 6.4	0.05
NCS	112.2 ± 4.8		126.6 ± 5.1	

Lympho-cytes	4 weeks	*P*	8 weeks	*P*	14 weeks	*P*
SHR	122.2 ± 5.7	NS	118.1 ± 3.2	NS	121.3 ± 5.0	0.05
WKY	124.5 ± 6.2		108.2 ± 5.1		99.4 ± 6.7	
Platelets	4 weeks	*P*	8 weeks	*P*	20 weeks	*P*
SHR	129.9 ± 8.2	NS	146.4 ± 8.6	0.001	170.6 ± 11.1	0.001
WKY	124.2 ± 8.4		103.1 ± 6.2		83.0 ± 7.5	

The following conclusions can be drawn: *(1)* $(Ca^{2+})_i$ is higher in hypertension than in normotension; *(2)* differences are more evident in platelets than in lymphocytes; *(3)* differences are greater in hypertensive rats than in humans in comparison with the respective normotensive counterpart; *(4)* abnormality of $(Ca^{2+})_i$ evolves roughly pari passu with the development of high blood pressure. Attempts were done to elucidate the mechanism of the increased $(Ca^{2+})_i$ in blood cells in HT. In lymphocytes, increasing $(Ca^{2+})_o$ led to a comparable, though slight, increase in $(Ca^{2+})_i$ in SHR and WKY; (SHR from 146 to 220 nm, WKY from 85 to 148 nm). Lowering $(Ca^{2+})_o$ to 100 nM again led to a comparable slight decrease of $(Ca^{2+})_i$ in SHR and WKY. Since the force driving the influx of Ca^{2+} into the cells and activating the outward Ca^{2+} pump should be abolished at 100 nM $(Ca^{2+})_o$, the higher $(Ca^{2+})_i$ in SHR under these conditions must be at least partly contributed by exchange with intracellular stores. Addition of cathecolamines in vitro produced no effects in $(Ca^{2+})_i$ in lymphocytes, thus discounting a role of this agent in abnormal cellular (Ca^{2+}) regulation. Addition of ouabain, increasing $(Na^+)_i$, had no effect on $(Ca^{2+})_i$ suggesting that at least in lymphocytes (Na^+) does not participate in $(Ca^{2+})_i$ regulation and to its alterations in HT. These results suggest a generalized defect of cytoplasmic (Ca^{2+}) control in HT. Investigations are now extended to tissues (synaptosomes and arterial myocytes) more directly involved in blood pressure regulation.

Increased urinary calcium excretion of hypertensive patients is due to a reduced tubular calcium reabsorption. *M. Cirillo, P. Strazzullo, A. Siani, F. Galletti, and V. Nunziata. Department of Internal Medicine, II Medical School, University of Naples, Naples, Italy.* Urinary calcium (Ca) excretion rate has been investigated in untreated essential

hypertensive patients with normal renal function and no target organ disease. Hypertensives ($N = 60$) showed significantly higher 24-hr urinary Ca excretion (+27%, $P < 0.01$), as well as increased levels of plasma parathyroid hormone (+28%, $P < 0.05$) and urinary cyclic adenosinemonophosphate (+33%, $P < 0.001$) compared to healthy normotensive controls ($N = 60$), while no difference was observed regarding serum Ca levels between the two groups. Urinary Ca excretion under fasting conditions was also higher (+40%, $P < 0.001$) in hypertensives ($N = 30$) than in normotensives ($N = 30$). In the course of a constant rate intravenous Ca load (15 mg Ca/kg body wt/3 hr) hypertensive patients ($N = 14$) had a higher urinary Ca excretion rate than control subjects ($N = 12$) at all levels of serum Ca and independently from the difference in glomerular filtration rate. The regression line of urinary Ca excretion rate on serum Ca level had in the hypertensive subjects a significantly increased slope (+35%, $P < 0.01$) compared to that of control subjects: This finding could indicate an abnormality in tubular Ca reabsorption in the proximal tubule. The theoretical threshold for renal Ca excretion (indicated by the x axis intercept of this regression line) was reduced, but not significantly, in hypertensive patients (−3%). As it was reported that parathyroid overactivity increases the value of the renal Ca threshold, we can hypothesize that the parathyroid activity, which is enhanced in hypertensive patients, compensates to some degree for a proximal Ca leak by increasing Ca reabsorption in the distal nephron. The basal phosphate clearance, somewhat higher in hypertensive patients (+15%, $P < 0.05$), makes rather unlikely the hypothesis that the tubular abnormality of these patients was located in the distal nephron. In conclusion, hypertensive patients had a higher urinary Ca excretion rate despite normal serum Ca levels and mild parathyroid overactivity: This abnormality seems to be due to an altered tubular Ca reabsorption probably located in the proximal tubule.

Blood pressure and exchangeable sodium during sodium depletion in normal subjects and in essential hypertensive subjects. *C. Zoccali, D. Davis, R. Fraser, J. J. Brown, A. F. Lever, and J. I. S. Robertson. Centro Fisiologia Clinica CNR, Reggio Calabria, Italy, and MRC Blood Pressure Unit, Glasgow, Great Britain.* In patients with essential hypertension arterial pressure is directly related to exchangeable sodium, but no such relationship has been found in normal subjects. A possible explanation of this phenomenon is that body sodium may change in normal subjects without a change of blood pressure but that in essential hypertensive subjects the same change of body sodium alters arterial pressure. We have measured blood pressure, exchangeable sodium, sodium balance, and plasma concentration of active renin and aldosterone in seven normal men and in ten essential hypertensive subjects of similar age and weight. Each subject was studied in two occasions: during a 3-day period of fixed, normal sodium intake (150 mmoles/day) and during a period of sodium depletion produced by a single dose of furosemide (40 mg) followed by 3 days of low sodium intake (10 mmoles/day). The order of the two periods was randomized. Sodium depletion caused a similar reduction of exchangeable sodium in the two groups (essential hypertensives: −7.1 ± 3.8%; normal subjects: −7.0 ± 3.3%) but, on the average, mean blood pressure changed more in essential hypertensives (−15 ± 12 mm Hg) than in normal subjects (+3.8 ± 6 mm Hg) ($P < 0.01$). The five patients showing the greatest arterial pressure fall had a lower rise of plasma renin (+179%) and aldosterone (+59%) in comparison with the five patients having the least arterial pressure change (renin +752%, aldosterone +178%). The findings are compatible with a model of pressure-natriuresis which alters more in normal subjects during changes of dietary sodium thereby preventing a rise of arterial pressure. Failure of this compensatory mechanism may raise blood pressure.

The acute antihypertensive effect of captopril and nifedipine is enhanced in the upright position by different sympathoinhibitory mechanisms. *A. Morganti, C. Sala, L. Turolo, A. Palermo, and A. Zanchetti. Institutes of Clinica Medica IV and IX, University of Milan and Centro di Fisiologia Clinica e Ipertensione, Ospedale Maggiore, Milan, Italy.* Both converting enzyme inhibitors and calcium antagonists have the potential of interfering with sympathetic nervous system activity; if this sympathoplegic action is relevant one might expect that their antihypertensive effect is potentiated by orthostasis. To define whether and how this indeed occurs, we measured systolic and diastolic blood pressures (SBP and DBP mm Hg), heart rate (HR b/min), plasma noradrenaline (NA pg/ml) and plasma renin activity (PRA ng/ml/hr) in the supine (S) position and after 30 min of upright (U) position, in 14 patients with essential hypertension before and after the oral administration of either 25 mg captopril (C) or 10 ng nifedipine (N). In control studies U and S SBP were similar whereas DBP, HR, NA, and PRA were always increased by U ($P < 0.01$ at least). The administration of C had no effect in S except that PRA was increased (from 0.8 ± 0.2 to 1.2 ± 0.4); in contrast, after U, SBP was always lower than in control studies (148 ± 6 vs. 167 ± 6, $P < 0.01$) and DBP was unchanged with respect to the values in S (103 ± 5 vs. 102 ± 3). Despite this depressor effect, after U both HR and NA values were similar to those before C (respectively, 84 ± 5 vs. 87 ± 4 and 453 ± 22 vs. 473 ± 40) whereas PRA was much higher (2.9 ± 0.8 vs. 1.3 ± 0.3). The administration of N lowered both SBP and DBP in S (from 165 ± 8 to 151 ± 6 and from 100 ± 5 to 92 ± 4, $P < 0.05$) and this effect was associated with significant increments ($P < 0.05$ at least) of HR (from 72 ± 3 to 83 ± 3), NA (from 291 ± 19 to 370 ± 20) and PRA (from 0.8 ± 0.2 to 1.0 ± 0.2). After U, SBP decreased further to 135 ± 5 whereas DBP remained as in S (95 ± 4); in addition HR, NA, and PRA increased more than in control conditions (respectively, to 101 ± 4, 620 ± 33 and 1.9 ± 0.3). In nine patients restudied again, according to the same protocol, after 5 days of diuretic therapy both C and N induced, again, an equal and additional depressor effect in U; however, while after C the U values of HR and NA were similar to those seen in control conditions (respectively, 89 ± 7 and 88 ± 4 and 645 ± 23 and 617 ± 27), after N both these parameters were clearly much higher (108 ± 5 and 731 ± 29, $P < 0.01$). The observation that the acute administration of C and N has a greater hypotensive effect in U than in S indicates that both these drugs interfere with the response of the sympathetic nervous system to the postural stimulus; however, while the sympathoplegic effect of C is apparently due to a blunted reflex activation, either centrally or peripherally, that of N seems dependent on a diminished vascular responsiveness to the adrenergic stimulus.

H_2 parathyroid receptors and 1-25$(OH)_2$ therapy in uremia on regular dialysis treatment (RDT). *F. Antonucci, P. Messa, D. Montanaro, M. Adorati, M. Messa, G. Paviotti, A. Favazza, G. Mioni, M. Cecchettin, and E. Bonucci. Servizio Nefrologia O.C. Udine, III Servizio Analisi O.C. Brescia, Istituto Anatomia Patologica Università Roma, Rome, Italy.* Our previous study evaluated the parathyroid gland response (PTH-NH_2 1-34) to an intravenous cimetidine load (200 mg) in 30 uremic patients on RDT with a variable degree of secondary hyperparathyroidism (HPT) proven by bone biopsy. Out of this population we selected three groups of five patients characterized by a decrease (group A), increase (group B), and unchanged (group C) PTH-NH_2 secretion. We treated all these patients with 1-25$(OH)_2$ for 12 months (0.25 to 1 μg/day). Serum Ca, sP, PTH-COOH(65-84), PTH-NH_2(1-84), and AP were measured before starting the treatment and every 3 months. Radiographic film of hands were obtained before and after the therapy. The patients as a whole showed an increase of sCa ($P < 0.05$), sP ($P < 0.01$), and a decrease of PTH-COOH ($P < 0.01$), PTH-NH_2 ($P < 0.01$), AP ($P < 0.01$). An inverse correlation between basal and maximal percent variations of sCa were found ($P < 0.01$). Furthermore, basal sCa levels inversely correlated with maximal percent variations of PTH-NH_2 ($P < 0.01$) and the variations of sCa resulted inversely correlated with percent variations of PTH-NH_2 ($P < 0.01$). When we considered the response to 1-25 treatment in the three groups, we found an early and significant fall of PTH-NH_2 ($P < 0.01$) in group A, no variations in group B and a late (ninth month) significant fall ($P < 0.05$) in group C. Alkaline phosphatase reduced in all groups ($P < 0.01$). Radiographic hand film showed a marked reduction of osteolysis in group A; on the contrary, in three patients of group B there was a clear worsening and no significant variations were observed in group C. The percent fall of PTH-NH_2 1-34 induced by cimetidine test in group A significantly correlated with the final percent fall of PTH-NH_2 1-84 produced by 1-25 in the same group ($P < 0.05$). We conclude that the sCa levels and the type of response to cimetidine test may be predictive of the effect of 1-25 on secondary HPT in patients on RDT.

Nitrogen balance and growth in children on hemofiltration. *M. Giani, M. Picca, I. Ghio, A. Saccaggi, R. Galato, L. Romeo, V. Cecchetti, and A. Edefonti. Pediatric Dialysis Unit, University of Milan, Milan,*

Italy. Malnutrition and wasting are commonly seen in uremic pediatric patients treated with hemodialysis (HD) and are reported to have an adverse effect on growth rate (GR). Such data are still lacking for hemofiltration (HF). Comparative influence of HD and HF on nitrogen balance (Nb) and GR was investigated in eight children (11.45 ± 2.8 years), treated first with HD for 25.7 ± 11.9 months and afterwards with HF for 21.6 ± 4.2 months. HF was prescribed on the basis of urea generation rate (Gu). Nb was evaluated every 2 months by the difference between dietary protein intake (DPI) and protein catabolic rate (PCR). There was no significant difference for energy and protein intake in HD compared with HF. Results were determined as mean ± (SD).

	Gu *mg/min*	PCR *g/kg/day*	Nb *mg/kg/day*	GR *cm/year*
HD	3.8 (0.9)	2.04 (0.6)	6.14 (124)	1.9 (1.1)
HF	2.7(0.43)	1.29 (0.5)	186 (97)	3.9 (0.4)
P	0.01	0.02	0.01	0.001

In conclusion, during the HF period, our patients improved their Nb and GR. Even if many other factors contribute to impaired growth, a positive Nb seems to play a key role to maximize growth potential.

Ultrasonically guided fine-needle alcoholization (UGFNA) as support to medical treatment of secondary hyperparathyroidism (sHPT). *A. Giangrande, P. Cantu', L. Solbiati, and C. Ravetto. General Provincial Hospital, Busto Arsizio, Italy*. sHPT frequently complicates the clinical course of chronic uremia, although more active vitamin D metabolites are now available. Parathyroid hyperplasia which sustains this pattern is seldom influenced by medical treatment and may require parathyroidectomy (PTX). As an alternative to surgery, in selected cases (single hyperplasia, uneffective subtotal PTX, seriously ill patient, refusal to surgery), we obtained a reduction of parathyroid mass by UGFNA. Ten out of 88 patients (3 M, 7 F, aged 34 to 69, on hemodialysis from 65 to 176 months) with symptomatic sHPT and positive US scan were treated with one infiltration of 0.6 to 1.2 ml sterile absolute ethanol introduced with a disposable needle (22G, 95 mm long). The US diagnosis was preliminarily confirmed with fine-needle aspiration biopsy and/or iPTH assay of aspirated material. The technique, always well tolerated, produced an evident change of echopattern already present after 1 to 2 weeks. In eight patients a remarkable reduction (up to 100%) of gland size was noted after 6 months from alcoholization, while the lesions were replaced by either fibrotic pattern or small liquid areas. With a single lesion, a reduced incidence of vitamin D hypercalcemia and a permanent improvement of bone alkaline phosphatase and iPTH was documented.

Intestinal absorption in nephrotic syndrome. *C. Pecoraro, M. Usberti, B. Guida, A. Romano, L. Grumetto, L. Carbonaro, A. Pinto, and M. T. Saravo. Pediatric Clinic and Department of Medical Nephrology, II Faculty of Medicine and Surgery, University of Naples, Napoli, Italy*. Intestinal absorption, as it has been recently shown in experimental animals, is decreased in nephrotic syndrome (NS). In this study we evaluated intestinal transport in a children's group with NS by techniques commonly used for this purpose in pediatric gastroenterology. Ten children (5 boys and 5 girls, mean age, 5.2 years) with NS and normal GFR were studied; none took steroid treatment and every therapy was stopped from at least 10 days at the study's time. Intestinal absorption was estimated by these tests: *(1)* D-xylose absorption test, *(2)* oral iron loading test, *(3)* oral triglycerides loading test. The results were compared to those of 12 children (7 boys and 5 girls; mean age, 4.5 years) without renal or intestinal pathology. Nephrotic children had significantly lower basal plasma albumin, serum iron, and transferrin levels, but higher plasma triglyceride levels than the control group. Serum xylose, iron, and triglyceride concentrations after respective loads were significantly lower in nephrotic children than in the control group, without a correlation between basal levels of these substances and their increase after the load. A statistically significant correlation was established between plasma albumin concentration and a rise in xylose ($P < 0.01$), serum iron ($P < 0.01$) and plasma triglycerides ($P < 0.05$) levels. Because intestinal epithelium is structural and functional similar to that of the proximal tubule, these results agree with the studies which have shown in NS tubular proximal absorption decrease for hypoalbuminemia and, therefore, for decreased plasma oncotic pressure in peritubular capillaries. Our study shows that intestinal absorption in NS is generally and not specifically decreased; the plasma albumin level may play an important role in decreasing intestinal transport, although the possibility exists that other factors are also involved.